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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/765,048	01/28/2004	Nobuhiko Nomura	04853.0111	9606

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EXAMINER	
FETTEROLF, BRANDON J	
ART UNIT	PAPER NUMBER
1642	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/27/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/765,048	NOMURA ET AL.	
	Examiner	Art Unit	
	Brandon J. Fetterolf, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 November 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11* is/are pending in the application.

4a) Of the above claim(s) *1-3 and 6-11* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4 and 5* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *28 January 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☒ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application Status

The previous Non-Final Office action mailed on 1/29/2007 has been withdrawn in favor of the instant Non-final Office Action because it was pointed out by Applicants that the Koo et al. reference cited in the previous Non Final Office Action was incorrect. As such, the instant Non-Final Office action corrects this "key" stroke error and incorporates the correct Koo et al. publication number.

Election/Restrictions

The Election filed on November 16, 2006 in response to the Restriction Requirement of October 16, 2006 has been entered. Applicant's election, with traverse, of Group II, claims 4-5, as specifically drawn to a method of screening for a substance inhibiting acylated homoserine lactone is been acknowledged. The traversal is on the grounds that the different groups would not require separate and distinct searches, and that it would not be burdensome to search the invention of all of the groups in light of the filing of only 11 claims and the existence of two groups (II and IV) with only 2 claims. Moreover, Applicants request that Groups II and III be combined since all of the claims of Group III (claims 6-7 and 9-10) depend form claims 4-5 of Group II. In addition, Applicants assert that since Groups III and II are related as product and process of use, process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined according to the provisions of M.P.E.P. 821.04. As such, Applicants respectfully request rejoinder of the nonelected product claims of Group III if a process claim of Group II is found allowable.

These arguments have been carefully considered, but are not found persuasive.

Regarding Applicants assertion with respect to searching, the Examiner recognizes that the inventions are classified differently, necessitating different searches of the US Patents. Further, classification of subject matter is merely one indication of the burdensome nature of the search involved. The literature search, particularly relevant in this art, is not coextensive and is much more important in evaluating the burden of search. Different searches and issues are involved in the examination of each group. Regarding Applicants request for rejoinder of the nonelected product claims of Group III if the elected process claims of Group II are found allowable, the Examiner

acknowledges that the MPEP states that process claims that depend from or otherwise include all the limitations of the allowable product claim will be rejoined according to the provisions of M.P.E.P. 821.04. However, the Examiner recognizes that Applicants have instead elected the process claims; and therefore, have lost their right to rejoinder under MPEP 821.04.

For these reasons, the restriction requirement is deemed to be proper and is therefore made FINAL.

Claims 1-11 are currently pending.

Claims 1-3 and 6-11 are withdrawn from consideration as being drawn to non-elected inventions.

Claims 4-5 are currently under consideration.

(Note: The Examiner apologizes for the inclusion of claim 4 in both Group I and II and intended claim 4 to be part of Group II only. The Examiner appreciates Applicants for pointing out this discrepancy.)

Priority

Acknowledgment is made of applicant's claim for foreign priority based on applications filed in Japan on 1/29/2003. It is noted, however, that applicant has not filed a certified copy of the JP 2003-21053 application as required by 35 U.S.C. 119(b).

Information Disclosure Statement

The Information Disclosure Statements filed on 7/20/2004 and 8/19/2004 are acknowledged. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement is being considered by the examiner. A signed copy of the IDS has been attached with the previous Non-Final Office Action filed on 1/29/2007.

Drawings

The drawings, e.g., Figure 14, are objected to under 37 CFR 1.83(a) because they fail to show the result of determining apoptosis in cells in the presence of acylated homoserine lactone by

chromatic condensation using Hoechst 3341 staining as described in the specification on page 9. Any structural detail that is essential for a proper understanding of the disclosed invention should be shown in the drawing. MPEP § 608.02(d). Corrected drawing sheets in compliance with 37 CFR 1.121(d) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. The figure or figure number of an amended drawing should not be labeled as "amended." If a drawing figure is to be canceled, the appropriate figure must be removed from the replacement sheet, and where necessary, the remaining figures must be renumbered and appropriate changes made to the brief description of the several views of the drawings for consistency. Additional replacement sheets may be necessary to show the renumbering of the remaining figures. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Color photographs and color drawings are not accepted unless a petition filed under 37 CFR 1.84(a)(2) is granted. Any such petition must be accompanied by the appropriate fee set forth in 37 CFR 1.17(h), three sets of color drawings or color photographs, as appropriate, and, unless already present, an amendment to include the following language as the first paragraph of the brief description of the drawings section of the specification:

> The patent or application file contains at least one drawing executed in color. Copies of this patent or patent application publication with color drawing(s) will be provided by the Office upon request and payment of the necessary fee.

Color photographs will be accepted if the conditions for accepting color drawings and black and white photographs have been satisfied. See 37 CFR 1.84(b)(2).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 4 is rejected under 35 U.S.C. 102(b) as being anticipated by Smith et al. (J. Immunol. 2001; 167; 366-374, IDS) as evidenced by Zimmerman et al. (Science 1999; 286: 1741-1744).

Smith et al. teach a method of determining the affects of 3-O-C12- HSL (N-3-oxododecanoyl homoserine lactone) on MAP kinases, comprising contacting 16HBE cells with a test substance in the presence of 3-O-C12-HSL and determining the activation of ERK (page 371, 1st column, 1st full paragraph to 2nd column). Specifically, the reference teaches that the test compound completely inhibited the induction of ERK by 3-O-C12-HSL (page 372, Fig. 8). Thus, while Smith et al. do not specifically teach that Erk is involved in the survival signaling pathway in which Akt is involved in, the claimed limitation does not appear to result in a manipulative difference in the method steps when compared to the prior arts disclosure because as evidenced by Zimmerman et al., phosphorylation of Raf by Akt inhibited the activation of the Raf-Mek-Erk signaling pathway and shifted the cellular response in a human breast cancer cell line from cell cycle arrest to proliferation (abstract). Thus, the Akt signaling pathway is inherently associated with Erk. Moreover, although Smith et al. do not explicit teach a method of screening for a substance inhibiting acyalted homoserine lactone, the claimed preamble does not appear to result in a manipulative difference between the active steps claimed and those disclosed by the prior art, i.e.., culturing animal cells with a test substance in the presence of acylated homoserine lactone and detecting inhibition of the survical signaling pathway in which Akt is involved in the cells.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claim 5 is rejected under 35 U.S.C. 103(a) as being unpatentable over Smith et al. (J. Immunol. 2001; 167; 366-374, IDS) as evidenced by Zimmerman et al. (Science 1999; 286: 1741-1744) in view of Koo et al. (US 2002/0054869, 2002).

Smith et al. as evidenced by Zimmerman et al. teach, as applied to claim 4 above, a method of determining the affects of 3-O-C12- HSL (N-3-oxododecanoyl homoserine lactone) on the MAP kinase signaling pathway, comprising contacting 16HBE cells with a test substance in the presence of 3-O-C12-HSL and determining the activation of ERK, wherein the test compound completely inhibited the induction of ERK by 3-O-C12-HSL. Smith et al. further teach that the test compound is PD98059 (page 371, 1st column, 1st full paragraph to 2nd column).

Smith et al. as evidenced by Zimmerman et al. do not explicitly teach that the inhibition of ERK is determined by detecting apoptosis.

Koo et al. teach that inhibition of the MAP kinase signaling pathway specifically triggers an apoptotic response in human cells (paragraph 0010). Koo et al. further teach that inhibitors of the MAP kinase signaling pathway such as PD9805 are useful for inhibiting the growth of a tumor in a mammal, wherein the inhibitor induces a cytotoxic response leading to apoptosis of cells in said mammal (Claims 16-20 of US 2002/0054769).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of the references so as to determine the affects of 3-O-C12- HSL (N-3-oxododecanoyl homoserine lactone) on the MAP kinase signaling pathway in the presence of a test compound as taught by Smith et al. by detecting apoptosis of the cell in view of Koo et al. with a reasonable expectation of success. One would have been motivated to do so because Zoo et al. teach that it is well known in the art that the inhibition of the MAP kinase signaling pathway triggers an apoptotic response in human cells; and further that inhibitors of the MAP kinase signaling pathway are well known to induce apoptosis.

Claims 4-5 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pearson et al. (US 5,591,872, 1997, IDS) in view of Tateda et al. (Infection and Immunity 2003; 71: 5785-5793, IDS).

Pearson et al. teach a method of selecting inhibitors of the autoinducer molecule, N-(3-oxododecanoyl)homoserine lactone, comprising contacting the autoinducer molecule with a suspected inhibitor, measuring the ability of the treated autoinducer molecule to stimulate the

activity of a selected gene then determining whether the inhibitor represses or enhances the activity of the autoinducer molecule (column 5, lines 46-55). The patent further teaches a method of inhibiting the infectivity of P. aeuriginosa and methods of treating an immuno-compromised host infected by P. aeruginosa, e.g., a person afflicted with cystic fibrosis (column 6, lines 22-26).

Pearson et al. do not explicitly teach that the method comprising culturing animal cells with the test agent and acylated homoserine lactone and detecting the inhibition of the survival signaling pathway which Akt is involved in, e.g., apoptosis.

Tateda et al. teach that the Pseudomonas aeruginosa autoinducer N-3-oxodocecanoyl homoserine lactone accelerates apoptosis in critical cell populations, macrophages and neutrophils (page 5792, 1st column, 2nd paragraph). The reference further teaches that N-3-oxodocecanoyl homoserine lactone induced apoptosis plays a crucial role in the pathogenesis of P. auruginosa infection (page 5792, 1st column, last sentence of 1st paragraph).

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to culture a test substance in the presence of N-3-oxodocecanoyl homoserine lactone as taught by Pearson et al. in an animal cell such as a neutrophil and to identify an inhibitor of N-3-oxodocecanoyl homoserine lactone by detecting apoptosis in view of the teachings of Tateda et al. One would have been motivated to do so because Tateda et al. teach that Pseudomonas aeruginosa autoinducer N-3-oxodocecanoyl homoserine lactone accelerates apoptosis in critical cell populations such as macrophages and neutrophils; and further, Tateda et al. teach that N-3-oxodocecanoyl homoserine lactone induced apoptosis plays a crucial role in the pathogenesis of P. auruginosa infection. Thus, one of ordinary skill in the art would have a reasonable expectation of success that by culturing a test substance in the presence of N-3-oxodocecanoyl homoserine lactone as taught by Pearson et al. in an animal cell such as a neutrophil and identifying an inhibitor of N-3-oxodocecanoyl homoserine lactone by detecting apoptosis in view of the teachings of Tateda et al, one would achieve an effective method of identifying a suitable inhibitor for the treatment of an immunocompormised host infected by P. aeruginosa, e.g., a person afflicted with cystic fibrosis.

Note: Applicant cannot rely upon the foreign priority papers to overcome this rejection because a translation of said papers has not been made of record in accordance with 37 CFR 1.55. See MPEP § 201.15.

Therefore, No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brandon J. Fetterolf, PhD whose telephone number is (571)-272-2919. The examiner can normally be reached on Monday through Friday from 7:30 to 4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Brandon J Fetterolf, PhD
Patent Examiner
Art Unit 1642

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